REMARKS

Claims 1 to 4, and 6 to 15 are in the application. Claim 5 has been cancelled. Claims 1 to 4, 6 to 9 and 11 to 13 have been amended. Claims 14 and 15 have been added. Support for the added and amended claims lies in the original claims as filed, or in the specification, on page 9, lines 20 to 32 through page 14, lines 1 to 14. No new matter is believed added. The title has been amended as suggested by the Examiner and a revised abstract, also as suggested by the Examiner accompanies this response.

Rejection under 35 USC § 112

Claims 5 to 13 are rejected under 35 USC § 112, first paragraph, as failing to comply with the enablement requirement. Applicants respectfully traverse this rejection.

The Examiner states that "the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." (Office Action 1¶, page 4).

The Examiner comments that the "claims are broad and drawn to many respiratory conditions." Applicant disagree with this statement. The method of use claim (claim 6 as amended), recites the requirement that the composition (of claim 1) inhibit the binding of acetylcholine to an acetylcholine receptor. This method is not tied to the treatment of a disease state, nor to a respiratory condition as so noted by the Examiner.

The Examiner also comments that Zirkle states these compounds are the preferred compounds of his study and gives in vitro data, that "we don't know how these compounds behave in vivo".

Applicants wish to remind the Examiner that *in vivo* data is not now, nor has ever been necessary to establish patentability of a compound or composition. In fact, no biological data is required in a patent specification. However, the specification does in fact provide to the skilled artisan four (4) assays which are directly related to supporting the method of use claims herein. The first two which appear on pages 5 and 6 of the specification are directed to *in vitro* assays, and the second two which appear in the specification on page 6, lines 26 to 31 through page 8, lines 1 to 15 are *in vivo* assays.

More specifically and to address the Examiners point on page 5, the first assay "Analysis of Inhibition of Receptor Activation by Calcium Mobilization" is clearly directed to inhibition of a M3 muscarinic acetylcholine receptor. The second binding assay, page 6, lines 16 to 24 will provide the pan muscarinic antagonism data against the M1 to M5 receptors. The Examiner in fact comments about the 5 distinct subtypes of receptors existing (Office Action, page 5, lines 11 and 12). Therefore, this assay is meant to address this very point. The skilled artisan would readily understand the significance of these two assays and the potential limitations of compounds tested therein.

The Examiner cites to a Lee et al. article on nonselective receptor antagonists atropine, ipratropium and oxitropium. In particular the article discusses Ipratropium. It should be noted that Boehringer Ingelheim markets Ipratropium as a bronchodilator in aerosol form to be used as a metered dose inhalant. The compound was approved by the FDA in 1986. Ipratropium is also marketed in combination with albuterol sulfate (a beta 2 adrenergic) in an aerosol form. The marketing materials associated with this compound treat it as a nonselective muscarinic antagonist. Therefore, contrary to the Examiners questions of selectivity on page 6, none of which are necessary for a compound to be approved for use as efficacious in the treatment of muscarinic receptor antagonism. No data on such selectivity is believed necessary. It is quite clear to the skilled artisan that the Examiners question while of interest scientifically perhaps are unnecessary to achieving a compound having the claimed utility herein.

In view of these remarks and amendments to the claims, reconsideration and withdrawal of the rejection to the claims is respectfully requested.

Rejection under 35 USC § 102

Claims 1 to 4 are rejected to under 35 USC § 102(b) as being anticipated by Zirkle et al. (J. Med. Pharm. Chem. 1962). Applicant respectfully traverses this rejection.

The Zirkle reference was abstracted by Chemical Abstract and appears as the CAOLD citation provided by Applicants from the PCT International Search Report (of this application) with the Registry numbers of the compounds abstracted therewith.

The Examiner points out a compound having Registry # 106655-97-4 as being "synthesized and evaluated for its anticholinergic activity" (Office Action, Page 3, 5¶).

Upon review of this article it is clear however, that the authors did not provide any synthetic evidence/experimentals to teach how to prepare a quaternary ammonium tropane. Tables I-VIII list the methyliodide (MeI) and methylbromide (MeBr) salts, as well as hydrochloride (HCl) salt for various compounds.

Further, the last paragraph before the experimental details on page 354 of the Zirkle article describes the author's excitement that the compounds XIa and XIIIc are active even though they are not quaternary tropanes.

It can only be considered an assumption as to what happened as there is no description of the making a MeI or MeBr salt in the text of the paper, nor in the experimental details. Perhaps the Chemical Abstract reviewer saw the description of a MeI and MeBr salt in the table and then presumed that these were describing a quaternary tropane analog.

The paper is not enabling to make a quaternary tropane salt, even if the Chemical Abstract reviewer is correct that the compounds were made.

However, in order to advance prosecution on the merits of this application, Applicants have amended Claims 1 to 4 to a composition which is suitable for use as in the respiratory tract of a mammal as an inhaled formulation.

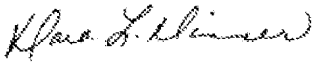
The Zirkle et al. article does not teach nor suggest that the compounds described therein are suitable for inhaled formulations, nor that the compounds as an inhaled formulations would be useful to treat M3 acetylcholine receptor mediated diseases.

Therefore, in view of these remarks and amendments, reconsideration and withdrawal of the rejection to the claims under 35 USC §102 over Zirkle et al. is respectfully requested.

CONCLUSION

It is believed that the claims, as amended, are now all in condition for allowance. Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned at the number below. It is not believed that this paper should cause any additional fees or charges to be required, other than expressly provided for already. However, if this is not the case, the Commissioner is hereby authorized to charge Deposit account 19-2570 accordingly.

Respectfully submitted,



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